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Investigating Gas Pepducin's Effect on β 2AR Signaling for CHF Pharmacology

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SKMC Class of 2021
SI CTR Abstract
12/15/18

Investigating G_{α_s} pepducin's effect on β_2 AR signaling for CHF pharmacology

Introduction: Congestive heart failure affects nearly six million Americans and significantly impairs their quality of life. New and better interventions are needed to improve HF patients' survival and outcomes. Pharmacologics that bias β_2 AR signaling towards arrestin, which promotes cardiomyocyte survival and contractility, may offer advantages over traditional β -blockers.

Objective: It has been demonstrated that peptides mimicking the C-terminus of the G_{α_s} subunit block downstream signaling of GPCRs. The study's objective is to determine if a pepducin derived from the C-terminus of the G_{α_s} subunit of the β_2 AR could block G_s signaling but maintain arrestin-recruitment, thereby producing a cardioprotective phenotype.

Methods: We used inverse PCR and bacterial transformation to design the peptide. We transfected Chinese hamster ovary (CHO) cells with the pepducin and used FACS and Glosensor assays to measure the concentration of cAMP in various cells.

Results: Results showed no inhibition of G_s signaling. Therefore, arrestin-recruitment was not tested.

Discussion: Previous researchers have demonstrated the results we failed to show, therefore we have reason to believe the peptide failed to inhibit G_s signaling because it is too small or too unstable. We are abandoning this line of research and will be continuing to approach the project's objective from new angles.